# THE WALTER AND ELIZA HALL INSTITUTE OF RESEARCH IN PATHOLOGY AND MEDICINE

# THE DIRECTOR'S EIGHTEENTH ANNUAL REPORT 1936-37

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1937

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Mr. A. M. Nicholas, who has represented the Walter and Eliza Hall Trustees on the Board of the Institute since 1931, died on 26th February last. We shall greatly miss him. Unhappily, owing to the state of his health, he has not been able to attend meetings of the Board during the last two years, but despite many calls upon his time he remained keenly interested in the work of the Institute, and helped us generously on numerous occasions.

# Historical Preface

The Walter and Eliza Hall Institute of Research in Pathology and Medicine was founded in 1916. The Trustees of the late Walter and Eliza Hall completed the Pathological Block of the present Royal Melbourne Hospital, and provided an annual payment of £2,500 towards the upkeep of the Institute. In 1925 this was increased to £3,100, and since 1930 has been £3,200 annually. In addition, the Institute has received, since its inception, £500 per annum from the University, the Medical Staff of the Melbourne Hospital having agreed that this portion of its clinical fund should be so used. Since 1925 a further sum of £250 per annum has been provided by the University from interest on the Appeal Fund (1924), together with an annual contribution from the Clinical Research Fund.

In 1926 the late Sir Aaron Danks, then President of the Melbourne Hospital, established an Endowment Fund to support a Biochemical Department. This fund has now reached the total of £8,591. The Edward Wilson Trustees maintained this new department by contributing £1,500 per annum in 1926, 1927 and 1928, and £1,000 in 1929. This Trust also, in 1926, contributed £3,000 for the foundation of an Institute Library, and of this sum £2,000 has been invested as endowment.

Since 1928 the Institute has been supported also by an annual contribution of £300 from the Felton Bequest Committee, and since 1933 by a contribution of £100 per annum from the Trustees of the late Anthony Mackie. The Trustees of the late T. J. Sumner have also helped to support the Institute since 1929.

The Institute has also received substantial support from the Department of Health of the Commonwealth Government; in the years 1927, 1928, 1929, 1930 and 1931 a total of £10,650 was received for special researches. In 1934 the Commonwealth Government entered into an agreement with the Rockefeller Foundation that each would contribute to the Institute the sum of £1,000 per annum for the ensuing three years to support work on Virus diseases, particularly those affecting the central nervous system.

In 1932, by the will of the late Mrs. L. E. W. Carty, of Brisbane Hill, Hamilton, the Elsie Marian Carty Fund was founded. Mrs. Carty willed to the Institute a portion of her estate and a residuary interest therein to establish this Fund. It was her wish that the income should be used, primarily, for the assistance of promising research workers.

From 1934 to 1937 Mr. A. M. Nicholas gave an annual sum of £250 towards the salary of the Assistant Director.

In 1936 the Carnegie Corporation of New York paid the travelling expenses of Dr. Feldberg, and have contributed in addition 4,500 dollars which, with £1,100 collected by Mr. Reuben Hallenstein, will be sufficient to support this worker until June, 1938.

In addition, a number of smaller gifts have been received from time to time from trusts and private individuals.

The Institute is controlled by a Board consisting of representatives of the Walter and Eliza Hall Trust, of the University of Melbourne, and of the Committee of Management and Medical Staff of the Royal Melbourne Hospital. During the war years Professor Sir Harry Allen acted as Honorary Director. In 1919 Dr. S. W. Patterson was appointed first Director; in April, 1923, he resigned, and was succeeded by Dr. C. H. Kellaway in August, 1923. During the interval Mr. H. Dew acted as Director.

# The Director's Eighteenth Annual Report

TO THE BOARD

OF THE

## Walter and Eliza Hall Institute of Research

IN PATHOLOGY AND MEDICINE.

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JULY, 1937.

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The Board of the Institute has lost three of its members this year. Our first serious loss was through the death of Mr. A. M. Nicholas, in February. In May, our President, Mr. Arthur Baillieu, resigned the Presidency of the Royal Melbourne Hospital. Finally Sir Frederick Mann, the Vice-President of the Board, resigned after his appointment as Lieutenant-Governor. We welcome the new President of the Hospital, Mr. B. T. Zwar, as President of the Board, and the two new members representing the Trustees of the Walter and Eliza Hall Trust—Mr. Russell Grimwade and Mr. Philip Aitken, both of whom have acted for the late Mr. Nicholas during his illness.

During the year the Institute has had a substantial output of research. This is the third year of the three-year period during which work on Virus diseases has been financed by grants from the Rockefeller Foundation and from the Department of Health of the Commonwealth Government. Happily these grants are being continued for a further period of two years.

The work of the Institute has been recognised by my invitation to deliver the Dohme Lectures at Johns Hopkins University Medical School at Baltimore in November, 1936. This necessitated my absence from the Institute for four and a half months, during which time Dr. F. M. Burnet acted as Director.

## DEPARTMENT OF VIRUS RESEARCH.

*Cultivation of Viruses on the Chorioallantoic Membrane.*

The quantitative study of virus phenomena by the chorioallantoic membrane technique continues to provide interesting results. Work has been extended to two new viruses—those responsible for the Rous sarcoma and for myxomatosis of rabbits —and further work has been carried out with viruses previously used, in particular, influenza, vaccinia and louping ill. The technique has now become standardised, and no important modifications were introduced during the year.

Since no comprehensive review of the method and the results obtained had appeared in the literature, a short monograph was prepared by Dr. Burnet, and has been published in the Special Report series of the Medical Research Council of Great Britain. It is of interest to note that since the manuscript of this monograph was forwarded to England, accounts of the cultivation of five additional viruses—lymphocytic choriomeningitis, St. Louis encephalitis, the common cold, smallpox and rabbit myxomatosis have been received. The wide utility of the method is thus becoming increasingly evident.

*Immunological Studies.*

The egg membrane technique is particularly suited to immunological work. Studies on laryngotracheitis, vaccinia, and influenza were mentioned in the last Annual Report. As further data were accumulated concerning the immunological reactions of these and other viruses certain general resemblances became apparent, and it seemed worth while to attempt a discussion of the general question of virus-antibody reactions centred round the egg membrane results. We have been working on this discussion throughout the year covered by this report, and much of the experimental work carried out in the department has been directed toward filling some of the gaps in our knowledge which a theoretical study of this sort always reveals. Of the viruses studied in detail, vaccinia and Newcastle disease viruses have been dealt with by Dr. Keogh, influenza by Dr. Burnet, while the work on laryngotracheitis and louping ill viruses has been done jointly by Dr. Burnet and Miss Lush.

With all these viruses, detailed quantitative experiments on the reduction in infectivity of virus suspensions by the action of appropriate immune sera have been carried out. The general conclusions reached may be indicated by the following summary:

1. Virus inactivation by immune serum results primarily from union of antibody to the virus surface. This union is a reversible one; it takes place at a rate and reaches an equilibrium determined by the ordinary laws of reversible chemical unions.

2. Union with antibody has no intrinsic inactivating effect on the virus; the inactivation is a result of the interaction between susceptible cell and antibody-coated virus particle. Certain susceptible cells are protected against infection by lesser degrees of antibody coating on the virus particle than are required by other types of cell.

3. In practice the experimental results obtained with any given virus will deviate from the theoretical values, owing to the operation of one or more of the following factors:

(a) Wide range of variation in the virus population in regard to susceptibility to inactivation by immune serum.

(b) The time required to reach equilibrium may be greater than that experimentally practicable.

(c) The lag between the time of inoculation and the initiation of an eventually demonstrable lesion by the primary infection of a susceptible cell may vary both in regard to the tissue inoculated and from individual to individual.

(d) Secondary reactions, particularly with concentrated reagents, may occur *in vitro* aggregation, secondary less readily reversible antibody-virus union and non-specific inactivation by environmental factors.

(e) When relatively large amounts of serum are inoculated, a corresponding degree of local and general passive immunity is produced which may prevent initiated infections developing to demonstrable lesions.

4. The aggregation and complement fixation reactions of viruses fall into line with the reactions of other antigens, the viruses finding a place in accordance with their particle size between soluble antigens and bacteria.

Arrangements have been made to publish this work in monograph form as a supplementary number of the "Australian Journal of Experimental Biology and Medical Science."

*Influenza Virus.*

The egg-adapted strain of influenza virus described in the last report has been further studied during the year, particularly from the immunological point of view. Two papers have been published dealing with the method of quantitative titration of the virus by the pock-counting method, and its application

to the study of the quantitative aspects of virus-neutralisation reactions. The results of this work have been already referred to in the section on general immunological work.

*(A) Absorption of Influenza Antibody.*

Study of the reactions of human and animal immune sera in other laboratories is gradually revealing certain complexities of the immunological behaviour of influenza strains. The nature of the difference between swine and human types of influenza viruses and the significance of the presence of swine influenza antibodies in human sera have given rise to particular difficulty.

Cross-absorption experiments naturally suggested themselves as a possible method for the study of such problems, and a beginning has been made with work of this sort. The technique has been to treat immune serum, suitably diluted, with infected mouse lung or egg membrane. The mixture is centrifuged, and the supernatant fluid heated to 56° C. for 30 minutes to inactivate any free virus. Heating usually causes some precipitation of tissue globulins, and a final centrifugation is carried out to clarify the material. This absorbed serum is then compared with serum similarly treated with non-infected tissues, by the usual methods of antibody titration.

With human, ferret, and horse immune sera the results have been consistent in showing that absorption removes a large proportion of the antibody which can be detected by egg membrane titration methods, but practically none of that responsible for the inactivation of mouse adapted virus. One ferret serum showed absorption of what may be called "mouse antibody" by infected mouse lung as well as of "egg antibody" by either mouse lung or egg membrane virus.

This dissociation of "egg antibody" from "mouse antibody" was unexpected, since comparative titrations of many sera by both methods had indicated a general equivalence between the two titres. It had been noticed, however, that high titre immune ferret sera had regularly shown proportionately higher titres by egg membrane titrations than in mouse titrations. As a provisional hypothesis we have adopted the view that influenza antibody is present in forms of varying avidity. Only the "highest grade" antibody is capable of preventing infection of the egg membrane. A tentative discussion of this conception has been given in the monograph by Burnet, Keogh, and Lush, and current work suggests that it is a valuable help in the interpretation of the results obtained in titration of human sera by different methods.

*(B) Other Strains of Influenza Virus.*

Through the courtesy of Dr. C. H. Andrewes, of Hampstead, and Dr. T. Francis, of the Rockefeller Institute, we have obtained most of the standard strains of virus isolated in other parts of the world. These include Shope's swine virus, and the human strains W.S. and B.H. (English), P.R.8 and Philadelphia (American), and two Russian strains. The swine influenza strain is the only one which has yet been studied in any detail. It has been propagated on the egg membrane for about 30 generations, and appears to be showing the same gradual increase in pathogenicity for the egg as was observed with the Melbourne strain. So far only rough titrations have been possible, but there seems little doubt that with further passage a strain will be developed which can be used for accurate titration of swine type antibody on the egg membrane.

Francis observed distinct differences between the two American strains P.R.8 and Philadelphia, the former showing some antigenic resemblance to the swine type. Dr. Burnet and Miss Lush have been able to confirm such difference, and to show that the Melbourne strain is indistinguishable from Philadelphia. More extensive comparative studies are planned, but have been temporarily shelved, owing to lack of a sufficient supply of mice.

*(C) Immunisation Against Influenza with Egg-adapted Virus.*

With repeated egg passage the Melbourne strain of influenza virus has lost almost all pathogenicity for the ferret, and has never developed any power to cause lung lesions in the mouse. Both species, however, may be solidly immunised against virulent influenza by the intra-nasal administration of living egg virus. In the work reported in a paper published this year, Dr. Burnet used only the mouse adapted Melbourne strain to test the immunity induced by egg virus. When the other strains became available, the more strenuous test of immunity to heterologous viruses could be applied. Ferrets immunised without symptoms by the administration of Melbourne egg virus were quite resistant to strains Philadelphia and P.R.8, although these were more highly pathogenic for control ferrets than the Melbourne mouse strain previously used. Mice immunised with egg virus, however, behaved differently. They were immune to Melbourne and Philadelphia strains, but not to P.R.8 and swine influenza strains.

An obvious extension from this work is to ascertain whether administration of this living attenuated virus to human subjects will confer immunity to epidemic influenza. Human beings

differ immunologically from ferrets and mice, since they have all been previously exposed at various times to infection by the influenza virus, and the problem is in general to enhance an existing immunity.

Since living virus is used, attempts at immunisation were started cautiously with a few volunteers. No evidence of any harmful effect has been observed in about fifteen persons inoculated by spraying egg virus up each nostril with an atomiser, and it is hoped to carry out such experimental immunisation on a moderately large scale during the present winter.

*(D) Complement Fixation in Influenza.*

Following up the work of Wilson Smith at Hampstead, Miss Lush has been studying the complement fixation reaction with influenza immune sera. A suitable antigen has been prepared from egg membrane material, using both the Melbourne strain and the partially adapted swine strain. Reproducible results are readily obtainable, and a wide range of experimental immune sera and human sera has been tested against both antigens. It has proved possible to show that with immune ferret sera swine and human type antibody can be differentiated, and that the strain P.R.8 again gives evidence of being intermediate between the two types. In human sera the complement fixing power for both human and swine type antigens appears to run almost parallel. An analysis of the relationships between egg titrations, mouse titrations, and complement fixation tests, using in each case human and swine type virus, for representative immune sera is in progress.

*(E) Antibody Content of Human Sera.*

A large number of titrations of human sera have been made, mostly by egg membrane methods, in connection with several problems.

(1) Titrations of sera taken at three or four monthly intervals from a small number of subjects show that there has been a steady fall in antibody level over the two years which have elapsed since the last Melbourne epidemic in the winter of 1935.

(2) Sera have been obtained from about forty patients suffering from a pyrexia of influenzal type, but unassociated with a widespread epidemic. Two samples of serum, the first taken during the illness, the second four weeks later, were titrated. In no instance was there a rise in influenza antibody.

(3) A series of 37 sera from infants and children under five years were obtained through the co-operation of Dr. S. W.

Williams. Of nineteen under two years old, sixteen contained no trace of antibody, three showed small amounts, probably of maternal origin. Amongst eighteen from two to five years old, only four were completely lacking in antibody. This provides a further indication that there has been no epidemic influenza in Melbourne since June and July, 1935.

A limited survey of human sera shows that antibodies against human and against swine influenza strains are distributed in Australia much as they are in England and America. Almost all adults possess demonstrable swine type antibodies. In children, the human type antibody predominates, but in several children under ten years, with relatively high human type antibody, there was sufficient antibody to protect mice against at least ten lethal doses of swine influenza virus.

These preliminary studies during an interepidemic period will provide a useful background for studying the immunological features of an epidemic when it occurs.

*Myxomatosis of Rabbits.*

The successful cultivation of this virus on the chorioallantois by Miss Lush is of particular interest, since it has been generally regarded as the most species-specific of all known viruses. Despite this specificity, subcutaneous oedema fluid from a typically infected rabbit gave a large number of well-developed focal lesions when tested directly on the egg membrane. The virus was readily propagated, and at least as far as the 26th egg passage has retained its power to produce fatal and contagious infection in the rabbit.

Pock-counting methods may be used for titration of the virus, but the range of variation in counts is rather higher than usual. The minimal infecting dose for the rabbit seems to be slightly smaller than that for the egg membrane. The virus is not highly pathogenic for the egg, and does not provoke lesions in the embryo proper. Retrogression of the lesions commences after three days.

Immune sera from rabbits recovering after contact infection with myxomatosis or immunised by infection with the Shope fibroma can be used for neutralisation experiments on the chorioallantois. The inactivating effect of one such convalescent serum has been studied in detail by Miss Lush. There is a general resemblance to the results obtained with vaccinia virus, but there are certain aberrant aspects which suggest that individual variation amongst the virus particles plays an unusually important part. In all this work Miss Lush has had the benefit of co-operation with Dr. L. B. Bull, of the

Council for Scientific and Industrial Research, who supplied the virus and made accommodation available in his laboratory for infected rabbits. Miss Lush is also collaborating with Dr. Bull on immunological work in relation to the possible susceptibility of Australian mammals to latent infection with the virus.

*Virus of Rous Sarcoma.*

The virus of Rous sarcoma No. 1 has been studied by the chorioallantoic technique during the past few months. Rous and Murphy, in 1912, showed that extracts of the tumour and cell free filtrates gave rise to tumours, histologically sarcomata, in the membranes of the developing chick. Such tumours arose only when the virus came in contact with mesodermal tissues. In the present study, using Burnet's method of inoculation, mesodermal tissues are not exposed to infection, the inoculum being dropped on to an intact ectodermal surface. It was noted that in the central portions of the membrane, where slight trauma may result in exposure of mesoderm, that sarcomata appeared, exactly resembling those described by Rous and Murphy. There were, however, other discrete rounded lesions, developing slowly, which histological examination showed to have arisen in the ectoderm. Successive transfers of the virus on the chorioallantoic membrane have been made, one of thirteen generations, after which the virus was lost, and one, still in progress, of eighteen generations. These ectodermal lesions closely resemble the discrete pocks formed by the other viruses studied by this technique. They differ from them firstly, in their slow development, taking a week to develop to macroscopic dimensions, as compared with one to three days for other viruses. Secondly, they present a malignant character, which differentiates them sharply from the lesions of other viruses. The epithelial cells which compose the lesions show active proliferation, are greatly enlarged and of abnormal appearance, and tend to invade the mesodermal tissue. This invasion is not accompanied by an inflammatory reaction, as is seen with other viruses, which have a necrotic, rather than stimulating, effect on the ectoderm. It is possible to titrate the Rous virus by enumeration of these lesions, and studies in such titration, and on the effects of sera produced against both the Rous virus and against normal fowl tissues are in progress. It is interesting to note that retransfer of membranes bearing lesions to the fowl invariably results in the appearance of typical Rous sarcomata, irrespective of whether cell free extracts or grafts of the infected membranes are used. If eggs so inoculated are allowed to hatch, the chicken develops sarcomata

within a short time. A progress report of these studies was presented at the inaugural meeting of the Victorian Society of Pathology and Experimental Medicine.

*Vaccinia Virus.*

The study of the immunology of vaccinia virus has been continued, using the chorioallantoic technique, and the findings reported previously have been repeatedly confirmed. The results of this work are embodied in the combined monograph.

One interesting point arose in respect of the time required for vaccinia virus to initiate infection on the chorioallantoic membrane. The technique used was to inoculate a number of membranes with similar doses of vaccinia emulsion, and at intervals varying from a minute to six hours to wash the surface of the membrane with measured volumes of serum saline. The washings were titrated for virus content on other eggs, and the washed membranes allowed to develop normally. Titration of the washings made it possible to calculate how soon the virus became firmly attached to the chorioallantoic cells. It was found that washing within five minutes allowed almost quantitative recovery of virus, but that the amount of virus so recoverable diminished steadily with time following inoculation, showing that fixation of all the virus particles firmly enough to resist washing is not immediate, but is a continuous process, many particles still remaining either free or loosely attached to the cell, while others are firmly fixed. It is interesting to note that repeated washing of the living membranes with successive 1 c.c. volumes of saline did not affect the development of the embryos. The washed membranes developed typical pocks, the numbers of pocks per membrane increasing the longer the time elapsing between inoculation of the membrane and the washing, thus checking with the results of titration of the washings. These findings are somewhat similar to those recently reported by Perdrau and Todd, who found that 10-14 hours' contact with susceptible cells is required before vaccinia virus is protected against the lethal action of ultra-violet light.

*Vaccinia Virus—Process of Disinfection by Formalin.*

The kinetics of disinfection of vaccinia virus by formalin was studied by the chorioallantoic technique. It was shown that the disinfection of a typical virus by formalin followed the same laws as have been established for bacterial disinfection. The main interest of this study was the demonstration of the suitability of the pock-counting methods for such investigations.

*Newcastle Disease Virus.*

This virus was one of the first to be studied in the developing chick by Burnet and Ferry (1934). It is lethal for the embryo, minimal doses invariably killing in 48 hours. Because of its rapid lethal action pocks similar to those produced by other viruses do not arise on the membrane under ordinary conditions. It was found that if membranes were inoculated with virus, and subsequently with immune fowl serum, that the life of the embryo was prolonged to four days. Under these conditions discrete lesions closely resembling those produced by influenza virus appeared. These eggs, in which the initiated infection was rapidly followed by treatment with immune serum, and which showed evidence of successful infection in the shape of typical lesions, invariably died, although their life was prolonged. The problem of how this extension of life is effected by immune serum is extremely interesting, but no satisfactory solution has yet been reached. A brief account of these studies is included in the monograph. It is intended to study this problem again at a later date.

*Q. Fever (Queensland Rickettsial Fever).*

During the last three years, about 30 cases of febrile disease in human beings have been observed in Queensland. The fever did not conform to any of the usual clinical types, and investigations along orthodox bacteriological lines could not establish its etiology. The disease has been provisionally referred to as Q. fever. Dr. E. H. Derrick, who was investigating these cases, found that a mild febrile reaction followed inoculation of guinea-pigs with blood taken from a patient at the height of his fever. This guinea-pig fever was indefinitely transmissible by blood or liver emulsion from guinea-pig to guinea-pig, but no obvious pathological changes could be detected. After recovery, the animals were immune either to infective guinea-pig liver or to infective blood from human patients.

Dr. Derrick suggested that we should study the nature of this infection, and provided us with material in the form of guinea-pig liver emulsion. Dr. Burnet had no difficulty in obtaining the same results in guinea-pigs, and likewise failed to demonstrate the presence of cultivable bacteria, leptospirae, rickettsiae, or protozoa in infective guinea-pig tissues. The agent was found to be filterable with difficulty through relatively permeable gradocol membranes. Tests were made with other species of laboratory animals. The rhesus monkey reacted with a well marked fever, and the blood taken during the febrile period was infective for guinea-pigs. Mice inoculated intraperitoneally were also susceptible, the evidence of

infection being great enlargement of the spleen, with moderate enlargement and distinct histological changes in the liver. The infection was only rarely fatal for mice. In sections and smears of the enlarged spleens, rickettsial bodies were observed, often in very large numbers. These were situated in the cytoplasm of cells in the splenic pulp, forming rather sharply outlined microcolonies of closely packed organisms. These microcolonies were often of considerable size, up to 10u across. The rickettsiae were of the usual minute bacillary form, and stained well by Castaneda's method, or with Giemsa.

Miss Freeman collaborated in the subsequent work with this infection, and showed by suitable cross immunity experiments that the infective agent in mouse spleens was identical with that in guinea-pig liver. After many mouse to mouse passages, enlarged spleens were sent frozen by air to Brisbane. They were found by Dr. Derrick to produce typical fever in normal guinea-pigs, but none in guinea-pigs immune to another strain of the infective agent, obtained initially from a different patient. All the evidence available is compatible with the assumption that the rickettsiae are the actual infective agents, but as in all such problems, final proof of identity is difficult to obtain.

In typical heavily infected mouse spleens the rickettsiae are present in such large numbers that by differential centrifugation in the angle centrifuge it is possible to obtain emulsions containing large numbers of rickettsiae and only a small amount of tissue debris. Preliminary experiments indicate that such emulsions are specifically agglutinable by convalescent sera from guinea-pigs and a monkey, and by one of the two convalescent sera from human cases of Q. fever which are available to us at present.

Should this indication be established by further work, a valuable means for epidemiological study of the human disease should become available.

Dr. Burnet and Miss Freeman have suggested "Queensland rickettsial fever" as a suitable name for this disease.

*Immunological Reactions of Bacteriophages.*

Parallel with the work on virus reactions, Dr. Burnet and Miss Lush have completed a re-examination of the immunological behaviour of a typical bacteriophage, C.16, and an attempt to provide a relatively complete interpretation of phage immunology has been made. Such an interpretation had to take into account the previously established facts that bacteriophages could be inactivated by certain derivatives of susceptible bacteria (P.I.A., phage inactivating agent) in a fashion which

showed close resemblance to inactivation by immune serum. Further experiments on this phenomenon have been carried out by Miss Freeman, who has been particularly concerned with the mutual influence of serum and P.I.A. on phages. Her most important result was that phage particles treated with very small concentrations of immune serum lost almost completely their susceptibility to inactivation by P.I.A. The implications of this experiment seem to be that the chemical groups on the phage particle surface which are responsible for union (1) with antibody, (2) with P.I.A., are intimately related.

The principal conclusions reached in regard to the phage-antiphage reaction were—(1) It results from specific union of the phage surface antigenic groupings to antibody. (2) More than one antibody molecule must be attached to an average phage particle to inactivate it. (3) The reaction is practically irreversible, its spread is directly proportional to the concentration of antiserum and is uniform over the early stages of the reaction, except with very dilute antiserum. (4) A proportion of unduly resistant particles is present in every phage population. (5) Phage inactivated by antiserum can still be absorbed by susceptible bacteria.

The most conspicuous difference between phage and virus antibody reactions is that the former are irreversible, the latter reversible. In other respects there are close similarities between the two reactions.

*Staphylococcal Polysaccharide in Relation to Bacteriophage.*

It is now generally accepted that many bacteriophages of the coli-dysentery and cholera groups unite specifically with the antigenic polysaccharide of the bacterial surface. Miss Freeman has extended this work to the staphylococcal group which has not been previously studied in this respect. She finds that a substance can be extracted from *Staph. aureus* showing typical P.I.A. activity, and that this can be purified by tryptic digestion, followed by alcohol precipitation. The purified substance gives no biuret reaction, shows a strong Molisch reaction, and gives rise to reducing sugars on hydrolysis, precipitates with staphylococcal agglutinating serum, produces an erythematous skin reaction in susceptible human beings, and retains full P.I.A. activity. On boiling with weak acid or alkali, the P.I.A. activity is lost, but specific precipitation is practically unaffected and its skin reactivity moderately reduced.

The interaction between staphylococcal P.I.A. and the susceptible Phage Au.2 followed the same lines as similar reactions with dysentery phages. The loss of susceptibility to P.I.A. by

treatment of phage with sub-inactivating amounts of antiphage serum could be equally well demonstrated.

*Investigations on H. pertussis.*

Miss Timmins has been working on some problems connected with the bacteriology of whooping cough. If mice are inoculated intranasally under anaesthesia with an emulsion of H. pertussis, they become infected. Those given large doses die in two or three days, with smaller doses a subacute bronchopneumonia develops which may or may not be fatal. Post mortem cultures from the consolidated lungs usually give a pure culture of H. pertussis, but there is a fairly high proportion showing secondary infection. Histological sections of these lungs show variable degrees of bronchopneumonia, but the most interesting feature is the massive accumulation of bacilli on the ciliated surface of the bronchiolar epithelium—the situation which is characteristic of the infection in human beings.

It was hoped that this syndrome might be used as a laboratory "model" of clinical whooping cough, for work on immunological aspects of the infection. Several small experiments showed a distinct prophylactic effect of preliminary inoculation of vaccines, but the results were very irregular, and obviously called for the use of large numbers of mice to establish significant results. Unfortunately other calls on our limited supply of mice have so far prevented any serious work on such problems.

Miss Williams and Miss Timmins have carried out some incidental work on the media most suitable for the production of large amounts of culture for vaccine production.

A research fund has recently been made available at the Children's Hospital for the investigation of the production of immunity to whooping cough. Dr. S. W. Williams has undertaken the clinical side of this work, and the Children's Hospital has appointed Miss Timmins to assist him. She will continue to work in Dr. Burnet's department under his direction, and will be responsible for the serological and bacteriological aspects of the problem.

F. M. Burnet:

"Influenza Virus on the Developing Egg":

II. "Titration of Egg Passage Virus by the Pock Counting Method." "Australian Journal of Experimental Biology and Medical Science," 1936, 14, 241.

III. "The 'Neutralisation' of Egg Virus by Immune Sera." "Australian Journal of Experimental Biology and Medical Science," 1936, 14, 247.

IV. "The Pathogenicity and Immunising Power of Egg Virus for Ferrets and Mice." "British Journal of Experimental Pathology," 1937, 18, 37.

"The Modern Outlook on Influenza," Royal Melbourne Hospital Clinical Reports, 1937, 8, 1.

"The Use of the Developing Egg in Virus Research." Special Report Series, Medical Research Council, London, No. 220.

"Virus Diseases: The Present Position." "Medical Journal of Australia," 1st August, 1936.

E. V. KEOGH:

"The Kinetics of Formalin Disinfection of Vaccinia Virus."

"Australian Journal of Experimental Biology and Medical Science," 1937, 15, 109.

F. M. BURNET and M. FREEMAN:

"A Comparative Study of the Inactivation of a Bacteriophage by Immune Serum and by Bacterial Polysaccharide."

"Australian Journal of Experimental Biology and Medical Science," 1937, 15, 49.

F. M. BURNET and C. TIMMINS:

"Experimental Infection with Haemophilus pertussis in the Mouse by Intranasal Inoculation." "British Journal of Experimental Pathology," 1937, 18, 83.

F. M. BURNET, E. V. KEOGH, and D. LUSH:

"The Immunological Reactions of the Filterable Viruses."

"Australian Journal of Experimental Biology and Medical Science," Special Number (in the press).

F. M. BURNET and MAVIS FREEMAN:

"Experimental Studies on the Virus of Q. Fever." "The Medical Journal of Australia" (in the press).

D. LUSH:

"The Virus of Infectious Myxomatosis of Rabbits on the Chorioallantoic Membrane of the Developing Egg."

"Australian Journal of Experimental Biology and Medical Science," 1937, 15, 131.

*Department of Physiology.*

*Cell Injury and the Liberation of Histamine.*—Since Dr. Feldberg arrived, on the 1st June last year, he has been engaged chiefly in studies concerning the liberation of histamine by various substances which cause cell injury. Apart from the demonstration of the liberation of histamine in anaphylactic shock in the guinea-pig and dog, evidence from animal experiments in support of Sir Thomas Lewis' theory concerning the liberation of histamine by cell injury, was lacking. This further evidence has been supplied by studies upon snake venoms, peptone, and staphylococcal toxin.

*Snake Venoms.*—Dr. Feldberg and I have continued the work on copperhead venom, which I commenced with Mr. Le Messurier, and have studied also the action of a viperine venom, that of *Crotalus atrox,* and of the venom of the Indian Cobra, *Naia naia.* All these were found to cause the liberation of histamine from the perfused lungs of the guinea-pig and cat. The venoms caused broncho-constriction, oedema of the lungs, and the appearance of coagulable protein and of histamine in the outflowing fluids. This histamine was shown to be part of the normal store in the lungs, and increasing doses of venom caused its liberation in increasing amounts. With large doses of the two more active venoms, those of the Australian copperhead and Indian cobra, almost all the lung histamine was liberated. There was a striking parallelism between the amount of histamine liberated and the degree of cell injury caused by the venoms as indicated by morbid changes in the lungs, and by the presence of coagulable protein in the perfusate. These observations provided an instance of graded liberation of histamine in response to cell injury of graded intensity.

In two further papers Dr. Feldberg and I have studied the effects of the venoms of the Australian copperhead and of the Indian cobra upon the systemic and pulmonary circulations in the cat, and have shown that the reactions present close similarities to those of histamine. After the intravenous injection of copperhead venom conditions of primary and secondary shock, similar to those observed with histamine, can be distinguished. Large doses of venom cause constriction of the pulmonary vessels, as indicated by a rise of pressure in the pulmonary artery. Histamine has a similar action upon the lung vessels. The venom also causes morbid changes in the lungs (collapse and congestion in the early stages and haemorrhage and oedema in the later stages) which, since histamine has much less effect on the lung tissues, must mainly be attributed to direct cell injury by the venom. We found great variation in the histamine content of the lungs of cats, and a

parallel variation in their sensitiveness to venom. In old cats, whose lungs are rich in histamine, the rise in pulmonary pressure and the morbid changes which follow the injection of venom are much more evident than in young cats whose lungs contain little histamine. The pulmonary vessels of these young cats are also relatively insensitive to histamine. After the injection of copperhead venom there occurs also an increase in the corpuscle concentration of the blood due to fluid loss from circulation, a phenomenon which is characteristic of histamine poisoning. Part of the fluid loss, after injection of this venom, takes place in the lungs, but the main loss is due to increased permeability of the peripheral capillaries.

After intravenous injection of the venom of the Indian cobra we have shown that there is an immediate profound fall of blood pressure due to obstruction in the pulmonary circulation. If this obstruction is overcome a gradual secondary fall, associated with the fluid loss from circulation, takes place. The effects of this venom on the circulation and on the lungs differ from those of the venom of the Australian copperhead, in that pulmonary constriction and morbid changes in the lungs are much more striking, that lung oedema accounts for a greater part of the fluid loss, and that this venom causes no immediate vasodilatation but instead, in large doses injected intra-arterially, causes transient constriction. Nevertheless we must assume, that during the later stages, vasodilatation with increased permeability of the capillary walls occurs, either as the direct effect of venom or of histamine liberated from the lung. We were able to show that the increase in corpuscle concentration of the blood was not contributed to by contraction of the spleen nor by fluid loss into the liver. There remained only the possibility that that part of the fluid loss which was not accounted for by oedema of the lung was due to loss from the peripheral capillaries.

These experiments throw new light upon the symptomatology of poisoning in man by these venoms. After the bites of viperine snakes the predominant feature is peripheral circulatory failure. After the bites of Australian colubrine snakes circulatory shock also complicates the picture. This is well explained by cell injury and liberation of histamine by these venoms. In poisoning by the bite of the Indian cobra, the curari-like action of the venom is more pronounced, but the changes found in the lungs after death resemble those we have described in cats following the injection of this venom.

*Staphylococcal Toxin and Peptone.*—Dr. Feldberg and Dr. Keogh have shown that staphylococcal toxin, after a latent period of some minutes, causes an output of histamine from

the perfused lungs in guinea-pigs and cats, which amounted to from 4 to 15 per cent. of the histamine content of the lungs. The various batches of toxin have been prepared, titrated, and concentrated by Dr. Keogh in the Virus Department. Dr. Feldberg and Dr. O'Connor, from Sir Stanton Hicks' laboratory, found that peptone also caused the liberation of histamine from perfused lungs. The histamine set free amounted to not more than 3 per cent. of the lung histamine in guinea-pigs, and not more than 10 per cent. in cats. These experiments provide experimental proof for the conception advanced by Sir Thomas Lewis that the symptoms produced by bacterial toxins and by peptone are due to cell injury and liberation of histamine.

A review of these experiments, as well as of other recent work on the physiology of histamine, has been contributed by Dr. Feldberg to the Festschrift for Professor J. Demoor, of Brussels.

*The Results of the Excision of the Venom Glands of Snakes.*

I have studied the effect of the excision of the venom glands in thirty tiger snakes. The survivors were observed for nearly $2\frac{1}{2}$ years. During life, tests were made of the functional capacity of the remaining parts of the venom apparatus, which after death were examined by serial sections. It was found that some snakes, in which ablation of the glands was complete, survived in good health for periods up to 850 days. These snakes shed their skins in normal fashion, usually three times a year, and their digestive processes were not obviously interfered with—food being digested completely in the normal time (5 days). There was no evidence of regeneration of the glands from duct tissue left at operation, nor was there any obvious hypertrophy of the supralabial mucous glands, which might have been expected had the secretion of these glands taken the place of venom. In this species, the secretion of the venom glands is not essential to digestion.

In contrast to the earlier observations of Phisalix and Bertrand on vipers, no change was observed in the normal toxicity of the plasma after removal of the glands. It did not appear therefore that the venom glands secrete poison from a toxic precursor normally present in the blood stream, or that they provide a poisonous internal secretion.

It is of interest that these snakes, though kept in a warm room throughout the year and not allowed to hibernate, still displayed some seasonal changes. During the winter months their appetite was poor, and they did not shed their skins.

*The Dohme Lectures.*

In the first of these lectures I reviewed briefly the established facts concerning the constitution of snake venoms, summarising Holden's studies on haemolysis, and discussed the possible therapeutic applications of venom. In the second, I discussed the work from this Institute on the peripheral actions of snake venoms—their curari-like action on voluntary muscle and on the diaphragm; their paralysant action on sensory nerve endings; their action in causing peripheral circulatory failure, and the significance of the liberation of histamine by snake venoms demonstrated in recent studies with Dr. Feldberg. The third lecture was devoted to the consideration of acquired and natural immunity to snake venom.

W. Feldberg and C. H. Kellaway:

"Liberation of Histamine from the Perfused Lung by Snake Venoms." "Journal of Physiology" (in the press).

"The Circulatory and Pulmonary Effects of the Venom of the Australian Copperhead (*Denisonia superba*)." "The Australian Journal of Experimental Biology and Medical Science," 1937, 15, 81.

"Circulatory Effects of the Venom of the Indian Cobra (*Naia naia*) in Cats." "The Australian Journal of Experimental Biology and Medical Science" (in the press).

W. Feldberg and E. V. Keogh:

"Liberation of Histamine from the Perfused Lung by Staphylococcal Toxin." "Journal of Physiology" (in the press).

W. Feldberg and W. J. O'Connor:

"The Liberation of Histamine from the Perfused Lung by Peptone." "Journal of Physiology (in the press).

W. Feldberg:

"Die Ergebnisse tierexperimenteller Untersuchungen uber die Physiologie des Histamins." Festschrift for Professor J. Demoor (in the press).

C. H. Kellaway assisted by Helen Wischusen:

"The Results of the Excision of the Venom Glands of the Australian Tiger Snake (*Notechis scutatus*)." "The Australian Journal of Experimental Biology and Medical Science," 1937, 15, 121.

C. H. Kellaway:

"The Charles E. Dohme Memorial Lectures at the Johns Hopkins University School of Medicine," November, 1936. *Snake Venoms*: I. "Their Constitution and Therapeutic Applications." II. "Their Peripheral Action." III. "Snake Venoms and Immunity." "Bulletin of the Johns Hopkins Hospital" (1937), 60, 1 and 159.

*The Biochemical Department.*

*Snake Venoms.*

Mr. Holden and Mr. Setter have completed their work on the ultraviolet absorption of snake venoms, and have further investigated the effects of inactivation by heat and by formalin.

The U.V. curves of some venom fractions having more restricted toxic effects were also determined. Attempts were made in the case of the venoms of the black snake and the copperhead to relate these curves to the haemolytic activities of the venoms. No connection could, however, be observed. It would appear that different portions of the venom molecules are concerned in these different effects.

*Blood Pigments.*

The equilibrium between methaemoglobin and acid haematin was studied by means of the ultraviolet spectrophotometer. It was found possible to reconvert 95% of acid haematin into methaemoglobin by suitable changes in the reaction of the solution, provided that the acid haematin had been prepared from methaemoglobin. When the acid haematin was prepared from oxyhaemoglobin, only 70% could be reconverted to methaemoglobin. This confirmed, by an independent method, the work of Anson and Mirsky on the reversibility of the denaturation of the blood pigment and its derivatives. Further work showed, however, that the percentage not recovered in the case of oxyhaemoglobin was lost owing to oxidation coupled to the oxidation of the reduced haematin during the conversion of oxyhaemoglobin to acid haematin.

A special apparatus was devised in which simple chemical reactions could be performed in an atmosphere of hydrogen carefully freed from the last traces of oxygen. In it reduced haemoglobin was converted to acid reduced haematin and reconverted to reduced haemoglobin. Provided no oxygen was admitted to the apparatus at any stage, the degree of reconversion was as great for reduced haemoglobin as for methaemoglobin. Other denaturing agents, such as alcohol

and sodium salicylate, give similar results. When hen egg albumin was used in place of haemoglobin, denaturation in the absence of oxygen was not followed by any reconversion to the native protein. The denaturation and renaturation of the protein of the blood pigment appears to form a special case, and cannot as yet be closely connected with the denaturation of proteins in general.

Mr. Holden is at present engaged in a study of the relationships between porphyrins and proteins in an endeavour to elucidate the discrepancy between Haurowitz's assertion that porphyrins only associate with globin by absorption in the same way that they do with other proteins, whereas Hill and Holden found evidence of definite chemical combination between porphyrins and globin.

Miss Bick has completed and published her work on protein determination. The method is proving most useful for rapid and accurate determination of coagulable proteins. She is at present studying the relationships between zinc ions and erythrocytes. The erythrocytes of some species are agglutinated by traces of zinc salts, and the process is reversible by repeated washing of the agglutinated cells.

Mr. Setter is engaged in a study of the effect of alcohol and of acetone on oxyhaemoglobin. Oxyhaemoglobins of different species show certain well marked differences in the effect of these organic solvents. The coagula formed differ apparently in composition and solubility in dilute acids and alkalies.

Our thanks are especially due to Professor W. A. Osborne for allowing us to have the use of a spectro-photometer, and to Miss Bick, who has worked in an honorary capacity in the Institute throughout the year.

H. F. Holden:

"The Absorption Spectra of Some Modified Snake Venoms." "The Australian Journal of Experimental Biology and Medical Science," 1936, 14, 121.

"Methaemoglobin, a Spectrophotometric Study." "The Australian Journal of Experimental Biology and Medical Science," 1936, 14, 291.

"The Denaturation of Haemoglobin." "The Australian Journal of Experimental Biology and Medical Science," 1937, 15, 43.

Marjorie Bick:

"Note on the Determination of Proteins Solution." "The Australian Journal of Experimental Biology and Medical Science," 1936, 14, 305.

*Clinical Research.*

*The Treatment of Haemorrhage.*

Dr. Ian Wood, the Marion Carty Research Fellow, has continued his work on acute haemorrhage, and has made a special investigation into the treatment of bleeding peptic ulcers. In conjunction with Miss Splatt progress has been made in the study of the biochemical changes which take place after severe haemorrhage, and of the results of massive blood transfusion. Many technical alterations have been introduced in the original apparatus described by Marriott and Kekwick for the continuous intravenous administration of citrated blood. An endeavour has been made to simplify and increase the margin of safety of this procedure. This work has been greatly aided by the able co-operation of Dr. Hilda Gardner and members of the Resident Medical Staff of the Royal Melbourne Hospital, who have devoted much time and thought to the many problems which have arisen. We are endeavouring to establish the highest standards of blood grouping, and of chemical purity and freedom from bacterial contamination of saline and other reagents.

Ian J. Wood:

"The Treatment of Haemorrhage." "British Medical Journal," 18th July, 1936.

"The Technique of Continuous Intravenous Administration of Glucose-Saline Solutions and Blood." "Medical Journal of Australia," 19th December, 1936.

*Storage of Blood for Emergency Transfusion.*

Dr. Hilda Gardner, Miss F. Eleanor Williams, and Dr. Ian Wood are investigating the methods of preservation and storage of human blood. By employing special technique blood can be kept for several weeks, and this will enable it to be obtained at a moment's notice for emergency transfusion. In the past lives have been lost owing to delay involved in typing the blood of the patient and the donor, and in the collection of blood from the donor. A depot of stored human blood would be of the utmost importance in times of war as well as in civil life.

*Paralytic Ileus.*

The treatment of paralytic ileus by continuous gastric aspiration with an indwelling stomach tube has been studied by Dr. Ian Wood, and records have been made of the fluid intake and output. A positive balance has been maintained in these patients by continuous intravenous infusion of glucose in Ringer's solution.

*Peptic Ulcer.*

Dr. R. J. Wright-Smith and Dr. Ian Wood are making a study of the cause of death in patients suffering from peptic ulcer. The macroscopic and microscopic changes noted post mortem have been correlated with the clinical and radiological findings, and an attempt is being made to suggest improved methods of diagnosis and treatment. A combined paper will be presented before the Victorian Branch of the British Medical Association in October of this year.

*Tetanus.*

Dr. Rothstadt and Dr. Ian Wood analysed the hospital results in the treatment of a series of 24 consecutive cases of tetanus. The mortality in this hospital since 1922 has been 70%, a figure which shows very little improvement upon treatment in the days before anti-tetanic serum was available. The authors recommend the principles recently set out by Cole and Spooner (1935).

L. E. Rothstadt and Ian J. Wood:

"Some Observations on the Treatment of Tetanus." Royal Melbourne Hospital Clinical Reports, 1936, 7, 12.

*Progressive Post-Operative Gangrene of the Skin.*

Mr. G. R. A. Syme and Dr. Lucy Bryce have presented a case of this condition, which has been fully worked out bacteriologically, partly in these laboratories, and partly in the Pathology Department at the University. The bacterial flora found in the peripheral part of the slough consisted of a short-chained streptococcus, B. coli, B. proteus, Cl. Welchii, and of diphtheroids. From the central growth also a mixed flora, chiefly of intestinal origin, was obtained. At the edge streptococci predominated. Experimental attempts to produce gangrene with these organisms failed.

G. R. A. Syme and Lucy Bryce:

"Progressive Post-Operative Gangrene of the Skin." Royal Melbourne Hospital Clinical Reports, 1936, 7, 108.

*Hospital Routine Services.*

*Bacteriology and Clinical Pathology.*

As hitherto the routine diagnostic tests in bacteriology, haematology, serology, and allergy have been carried out. The number of tests performed was 15,920 for 10,294 patients.

These included 3,399 Wassermann tests and 134 gonococcal complement fixation tests. The allergic tests numbered 2,116 for 103 patients. Desensitisation was undertaken in some cases.

Dr. Gardner has co-operated with Dr. Bolton, the Medical Superintendent, in the diagnosis of cases of pneumonia admitted to the hospital within four days of the onset of the illness. The type of the invading pneumococcus was ascertained, where possible, by the Neufeld method, and this was confirmed by cultural tests, and the accompanying flora determined. Progressive leucocyte counts were also estimated in these patients. Selected cases were treated with appropriate vaccines.

Miss Williams has again been responsible for the hydatid complement fixation tests and for some of the serological tests during Dr. Gardner's absence. Dr. Wright Smith has carried out the Casoni tests for hydatid, of which there have been 22 positive results in 192 patients.

Dr. Gardner was granted two months' sick leave from 2nd February, and during her absence Dr. Heseltine, who had been Resident Assistant Clinical Pathologist during the previous twelve months, acted as *locum tenens.*

Dr. A. V. Jackson was appointed Resident Assistant Clinical Pathologist on 1st February, 1936.

Hilda J. Gardner:

> "The Determination of Blood Compatibility Before Blood Transfusion and Avoidance of Subsequent Reactions." "Medical Journal of Australia," 19th December, 1936.

*Biochemistry and Basal Metabolism.*

The work of this department has shown a steady increase in volume. This increase, with our limited room accommodation for patients, is difficult to handle efficiently.

Miss Marjorie Bick, B.Sc., spent three months in the department learning methods, and during that time rendered valuable assistance in the general work—and particularly in the special investigations required for cases of haematemesis.

We have used Quick's hippuric acid test for liver function in some fifty patients, but are not yet in a position to assess its value.

We have estimated the blood cholesterol at the same time as the basal metabolic rate in a small series of patients, but have not been able to show any constant relationship between the results of these two tests.

Miss Splatt will be leaving for England next September, having been granted a year's leave of absence, to enable her to gain further experience in clinical biochemistry in London. Her place will be filled temporarily by Miss Verney South, who was a voluntary assistant in this department in 1935, and who has worked under Professor E. C. Dodds at the Courtauld Institute, Middlesex Hospital, for the past year.

*Electrocardiography.*

During the year 790 electrocardiograms have been taken. The "Matthews" portable instrument, presented by the ladies of the Box Hill and Mont Albert Auxiliary in 1932, has been used by Mr. Hughes, who is in charge of this work.

*Morbid Anatomy.*

During the year 474 autopsies were performed. Dr C. H. Mollison and Dr. Wright-Smith were responsible for the examination of biopsies, which numbered 974. The routine photography, clinical and pathological, and photomicrography have been done by Miss Helen Wischusen.

*Coronary Obstruction.*

Dr. Wright-Smith has analysed a series of 495 autopsies upon persons who had died from this disease. Of these, 339 occurred in medico-legal and 156 in hospital practice. In more than half there was no record of symptoms attributable to coronary occlusion before the fatal attack. The underlying basis of the disease is atherosclerosis of the coronary arteries, and, as has been recognised, vascular syphilis is very rarely a cause of obstruction. Embolism is also extremely rare. The final fatal blockage was due to thrombosis in only 9 per cent. of the whole series (approximately only 7 per cent. in the medico-legal group, and about 13 per cent. in the hospital group). When thrombosis occurred there was always extensive atherosclerosis of the coronary vessels.

In this paper, in which the resultant morbid changes in the heart muscle are carefully described, emphasis is placed on the relative infrequency of thrombosis as a fatal termination. Atherosclerosis of the coronaries is gradual in its onset, but is often sudden in its manifestations, and fatal occlusion frequently occurs without any thrombosis.

R. J. Wright-Smith:

"Coronary Obstruction." Royal Melbourne Hospital Clinical Reports, 1936, 7, 71.

*Neuropathology.*

In conjunction with clinical work in neurology, Dr. E. Graeme Robertson has examined many specimens obtained at operation, or by Dr. R. J. Wright-Smith at post mortem. With the co-operation of his colleagues on the Honorary Medical Staff, patients with nervous diseases are being fully investigated in the wards. The material obtained at operation is sectioned, and a complete diagnosis can thus be established. Those cases which come to autopsy are studied both macroscopically and microscopically, and an analysis of clinical signs and symptoms is thus possible. A number of unusual lesions have been recorded. Our thanks are especially due to Dr. J. M. Lewis, who lent us a microtome for cutting celloidin sections, until a similar instrument could be imported from Vienna. Further development in this work will be possible thanks to a recent anonymous gift of £500 for research on diseases of the nervous system.

At the Auckland meeting of the Royal Australasian College of Surgeons in January, Dr. Robertson gave a lecture on intracranial Aneurysms. He briefly reviewed the symptomatology of the condition, as displayed by 41 cases observed at this hospital since 1929, and illustrated the difficulties of surgical treatment by the fuller discussion of some of these.

E. Graeme Robertson:

"Intracranial Aneurysms." "Medical Journal of Australia," 19th September, 1936, 381.

"A Clinico-pathological Demonstration." Royal Melbourne Hospital Clinical Reports, 1936, 7, 61.

*Museum.*

New specimens added to the museum included lipomata of the oesophagus, sarcoma of the stomach, carcinoid of the appendix, cysts of the pancreas, silicosis of the lungs, mediastinal teratoma, chorionepithelioma of uterus, carcinoma of uterus and congenital intracranial aneurysm. We are indebted to Dr. C. H. Mollison and Dr. R. W. Chambers for gifts of specimens.

*Teaching.*

The course of lectures and demonstrations arranged this year by the Melbourne Permanent Postgraduate Committee included two lectures by Dr. Ian Wood on the technique of blood transfusion and on the treatment of paralytic ileus, and two clinico-

pathological demonstrations by Dr. E. Graeme Robertson on changes in the visual fields produced by neoplasms and on tumours in the posterior cranial fossa.

Dr. Wright-Smith has given the usual course of lectures in pathology to fourth year students in January and February. Lectures in bacteriology were given to student nurses in the Hospital, and demonstrations of pathological material were given to the honorary staff at clinical meetings through the year.

Dr. Graeme Robertson, last year, gave a series of weekly clinico-pathological demonstrations to students on neurological cases. These will be recommenced in the second term of this year.

Dr. Hilda Gardner has as usual conducted the teaching of clinical pathology for fifth year students.

*The Library.*

Our thanks for the gift of journals and books are due to the following:—L'Académie Royale de Médecine de Belgique; The Cancer Research Committee, Sydney; The Commonwealth Department of Health; The Council of Scientific and Industrial Research; Miss Danks; Mr. Dobell, F.R.S.; Dr. Keith Fairley; The Government Institute for Infectious Diseases of the Tokyo Imperial University; The London Hospital; The Medical Research Council; The Middlesex Hospital Medical School; New York State Department of Health, Division of Laboratories and Research; Dr. R. J. Wright-Smith; La Société Royale des Sciences Médicales; The South African Institute for Medical Research; The University of Harvard, Department of Tropical Medicine; The University of Pennsylvania, Department of Pathology; The University of Tomsk.

CHARLES H. KELLAWAY,

Director.

# The Walter and Eliza Hall Institute of Research in Pathology and Medicine

## FINANCIAL STATEMENT FOR THE YEAR ENDED 30th JUNE, 1937.

### RECEIPTS.

| | | | | | | |
|---|---|---|---|---|---|---|
| To Balance brought forward from 30th June, 1936 | | | | £3,556 | 14 | 2 |
| ,, Trustees, Walter & Eliza Hall Trust | £3,200 | 0 | 0 | | | |
| ,, University of Melbourne | 750 | 0 | 0 | | | |
| ,, Felton Bequest Committee | 285 | 0 | 0 | | | |
| ,, Trustees late Anthony Mackie | 85 | 0 | 0 | | | |
| ,, Trustees late T. J. Sumner | 8 | 0 | 0 | | | |
| ,, Fees Received and Proceeds of Materials Supplied | 383 | 10 | 8 | | | |
| ,, Interest | 89 | 4 | 1 | | | |
| | | | | 4,800 | 14 | 9 |
| | | | | £8,357 | 8 | 11 |

### EXPENDITURE.

| | | | | | | |
|---|---|---|---|---|---|---|
| By Salaries and Wages | £4,158 | 2 | 1 | | | |
| ,, Materials | 347 | 11 | 6 | | | |
| ,, Apparatus | 64 | 14 | 7 | | | |
| ,, Sundries | 165 | 3 | 7 | | | |
| ,, Repairs to Apparatus | 11 | 17 | 3 | | | |
| ,, Repairs to Buildings | 4 | 2 | 4 | | | |
| ,, Publications | 67 | 13 | 5 | | | |
| ,, Fittings and Equipment | 42 | 19 | 11 | | | |
| | | | | £4,862 | 4 | 8 |
| ,, Biochemical Department | | | | 431 | 15 | 10 |
| ,, Library Account | | | | 23 | 7 | 9 |
| ,, Virus Account | | | | 363 | 11 | 9 |
| ,, Balance | | | | 2,676 | 8 | 11 |
| | | | | £8,357 | 8 | 11 |

### THE ELSIE MARION CARTY ACCOUNT.

| | | | | | | |
|---|---|---|---|---|---|---|
| To Balance brought forward from 30th June, 1936 | | | | £111 | 1 | 10 |
| ,, Interest | | | | 167 | 12 | 0 |
| | | | | £278 | 13 | 10 |

| | | | | | | |
|---|---|---|---|---|---|---|
| By Publications | £1 | 17 | 8 | | | |
| ,, Sundries | 3 | 10 | 5 | | | |
| ,, Salaries | 150 | 0 | 0 | | | |
| | | | | £155 | 8 | 1 |
| ,, Balance, Bank of New South Wales | | | | 123 | 5 | 9 |
| | | | | £278 | 13 | 10 |

## BIOCHEMICAL DEPARTMENT ACCOUNT.

| | | | | | | |
|---|---|---|---|---|---|---|
| To Interest transferred from Endowment Account | | | £393 | 18 | 3 | |
| „ Transfer from Income Account | | | 431 | 15 | 10 | |
| | | | £825 | 14 | 1 | |
| By Salaries and Wages | | | | | | £825 14 1 |
| | | | | | | £825 14 1 |

## LIBRARY ACCOUNT.

| | | | | | | |
|---|---|---|---|---|---|---|
| To Interest on Investments | | | £86 | 4 | 0 | |
| „ Transfer from Income Account | | | 23 | 7 | 9 | |
| | | | £109 | 11 | 9 | |
| By Books, Journals and Bookbinding | | | | | | £109 11 9 |
| | | | | | | £109 11 9 |



## VIRUS ACCOUNT.

| | | | | | | |
|---|---|---|---|---|---|---|
| To Commonwealth Government | | | £1,000 | 0 | 0 | |
| „ Rockefeller Foundation | | | 1,000 | 0 | 0 | |
| „ Debit Balance— | | | | | | |
| Income Account | £363 | 11 9 | | | | |
| Bank of N.S.W. | 168 | 17 6 | | | | |
| | | | 532 | 9 | 3 | |
| | | | £2,532 | 9 | 3 | |
| By Debit Balance brought forward from 30th June, 1936 | | | | | | £96 11 5 |
| „ Materials, Apparatus and Equipment | | | | | | 884 11 1 |
| „ Salaries and Wages | | | | | | 1,551 6 9 |
| | | | | | | £2,532 9 3 |

## PHYSIOLOGICAL RESEARCH ACCOUNT.

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| To Balance brought forward from 30th June, 1936 | £1,478 | 14 | 7 | By Apparatus | £323 | 11 | 10 | |
| „ The Carnegie Corporation, New York | 635 | 2 | 5 | „ Equipment | 15 | 8 | 0 | |
| „ Interest | 16 | 10 | 4 | „ Materials | 85 | 5 | 10 | |
| | | | | „ Sundries | 3 | 12 | 10 | |
| | | | | „ Salaries and Wages | 903 | 6 | 3 | |
| | | | | | | | £1,331 | 4 9 |
| | | | | „ Balance, Bank of New South Wales | | | 799 | 2 7 |
| | £2,130 | 7 | 4 | | | | £2,130 | 7 4 |

## FUND FOR NEUROLOGICAL RESEARCH.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| To Donation | £500 | 0 | 0 | By Balance, Bank of New South Wales | £500 | 0 | 0 |

## ENDOWMENT FUNDS.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| To Balance Biochemical Endowment Fund | £8,591 | 10 | 3 | By Investments | £14,846 | 1 | 0 |
| „ Balance Elsie Marion Carty Fund | 4,233 | 15 | 3 | „ Bank of New South Wales | 9 | 4 | 6 |
| „ Balance Library Fund | 2,030 | 0 | 0 | | | | |
| | £14,855 | 5 | 6 | | £14,855 | 5 | 6 |

I have to report that I have completed the Audit of the Books and Accounts of the Institute for the period ended 30th June, 1937. I have verified all receipts and have had vouchers produced for all disbursements. All information and explanations required have been given. The Statement is a correct statement of Receipts and Expenditure as revealed by the books of the Institute.

13th July, 1937.

W. M. JARVIE, F.C.A. (Aust.), Auditor.